TUMORS ON THE SPINAL CORD: THEIR DIAGNOSIS*

AN ANALYSIS OF FIFTY-NINE CASES

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THE object of this paper is to present the outstanding clinical features noted in a study of the last fifty-nine cases of tumor of the spinal cord seen at the University of California Hospital.

The first successful removal of a tumor of the spinal cord was accomplished by Sir Victor Horsley in 1887. Since that time our clinical knowledge of the subject has broadened, and many diagnostic aids have been established, the most valuable of which are the spinal puncture (simplified and perfected by Quincke in 1891) and its adaptation by Queckenstedt, in 1916, to the study of the hydrodynamics of the spinal fluid. Of these the Queckenstedt test is the more important. Its application permits recognition of partial or complete obstruction in the spinal fluid pathways.

Froin, in 1903, associated xanthochromia and coagulation (with or without an increase in the cell count) with a mechanical obstruction to the spinal fluid pathways. Seven years later, however, Nonne demonstrated that in such lesions an increase in the amount of globulin may be the only alteration.

The cisternal puncture (Ayer, 1920), and the combined cisternal and lumbar punctures offer a method of visualizing the altered hydraulics, and permit chemical and physical studies of the fluid removed from above and below the lesion. In 1923, Cushing and Ayer reported xanthochromia, as well as alterations in the amount of protein, both above and below tumors of the cauda equina. This finding deserves special mention because it is usually believed that xanthochromia occurs only below the level of the tumor.

Roentgenographic studies frequently demonstrate significant alterations in the vertebrae, such as narrowing of the pedicles, enlargement of the bony spinal canal or intervertebral foramen.

Lipiodol as a *localizing agent* (1922) has proved to be of great advantage in certain cases.

In 1931 we noted that bilateral compression of the jugular and other cervical veins enabled us to differentiate between radicular pain produced by gross intraspinal, space-consuming lesions, and extraspinal pain of radicular type.

In the differential diagnosis of tumors of the spinal cord it may be necessary to employ one or all of the diagnostic aids mentioned above.

AUTHORS' STUDY OF RECENT CASES

In our study of the last fifty-nine cases of tumor of the spinal cord and cauda equina at the University of California Hospital, we noted certain clinical peculiarities and characteristics associated with the various pathologic types of tumor. It is the object of this paper to present certain outstanding clinical features of the various types of tumor, according to location and pathologic classification.

The early diagnosis of tumors of the central nervous system is of utmost importance. Little can be accomplished by the surgical removal of a benign tumor if permanent damage to the cord has already occurred. In the group of patients with benign encapsulated tumors, 79.5 per cent received an excellent result. The average duration of partial or complete compression of the spinal cord was five and one-half months. Of the 20.5 per cent in whom the results were not satisfactory, the average duration of complete or almost complete loss of motor and sensory function was two years and four months.

Tumors arising from the spinal cord, meninges, nerve roots, and dura give early evidence of their presence. In our series, regardless of the type or location of the tumor, *pain* was the most common and usually the initial symptom. It often was present for a number of years before neurologic signs appeared. The pain often simulated that of other disorders, and the patients complained of rheumatism, neuritis, sciatica, lumbago, sacro-iliac strain, and abdominal symptoms. In the early stages the pain was invariably localized. In most instances it later developed into a combination of localized and radiating pain. When radiating pain appeared early it was unilateral, but eventually became bilateral late in the course of the disease.

Sensory alteration, motor weakness or disturbances of the sphincters were unusual as initial symptoms. In all cases the symptoms and signs could be explained on the basis of a single, progressive, space-consuming lesion.

The pathologic type and clinical peculiarities of the tumors in the series are of great interest.

HOUR-GLASS TUMORS

The first group is composed of the so-called hour-glass type of tumor. These tumors have an intraspinal portion connected by a small neck with an extraspinal enlargement. In our cases the connection occurred most frequently through an intervertebral foramen, but occasionally through an interlaminal space. It is generally accepted that hour-glass tumors are rare, yet there were fifteen such cases in this series.

The most important, single, subjective complaint in this group was localized pain, the duration of which varied from two weeks in one case to ten years in another. No pain was present in four cases. In general, the neurologic signs appeared relatively late and were characteristic of compression of the spinal cord.

Palpation of the extraspinal portion of the tumor was possible in the cervical region, and occasionally in the thoracic and lumbar regions. Roentgenograms of the spine proved extremely valuable. In addition to anteroposterior and lat-

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eral exposures, special views should be taken to show the intervertebral foramina. Enlargement of the latter structures frequently was demonstrated as well as erosion of transverse processes, laminae or dorsal surfaces of the bodies of the vertebrae, or a shadow cast by the extraspinal portion of the tumor itself.

In the fifteen cases the commonest pathologic types were neurofibroma, dural endothelioma, and hemangio-endothelioma. There was one osteochrondroma.

A preoperative diagnosis of this peculiar method of growth is important. In the absence of positive neurologic findings, a diagnosis of intrathoracic tumor has been made, and the intrathoracic portion of an hour-glass tumor removed without appreciating its character. Such mistakes have resulted in hydrothorax from a tearing of the dura with the escape of clear cerebrospinal fluid. The majority of hour-glass tumors are slow-growing and many can be enucleated.

INTRAMEDULLARY AND EXTRAMEDULLARY EXTRADURAL TUMORS

The intramedullary tumors in the proved cases were gliomas. In each instance they were very extensive and demonstrated the characteristic infiltrating properties, making complete surgical removal impossible, although large portions sometimes were removed with improvement. Pain of the same type as that found in other cases of tumor was the initial symptom. The average duration of pain was a year and a half, but in one case pain was present for six years. In one case laparotomy had been performed because of the severity of the referred pain.

The differential diagnosis between intramedullary tumors and extramedullary intradural tumors is difficult as a rule. In our cases, however, one differential point proved to be of value.

In the *extramedullary* tumors there was usually a clear-cut history of gradually increasing compression of the spinal cord. In these cases the sensory level was almost always sharply demarcated, and tended to be more pronounced in the distal part of the lower extremities than in the higher segments corresponding to the level of the lesion.

In the *intramedullary* tumors the reverse was true—that is, the maximum sensory loss corresponded to the segments of the cord immediately involved, while the sensory alteration in the distal parts of the extremities was not so marked. In addition, in an intramedullary growth, the sensory findings tended to fade off above the level of the tumor in a more or less indefinite fashion.

TUMORS OF THE CONUS MEDULLARIS

Involvement of the conus medullaris by either an intramedullary or an extramedullary tumor led, in all instances, to early involvement of the sphincters and varying degrees of impotence.

TUMORS OF THE CAUDA EQUINA

In this study, tumors of the cauda equina formed the most interesting but the most difficult diagnostic problems. Many of the old-established diagnostic principles were further emphasized, and new diagnostic points were revealed.

The majority of the primary tumors of the cauda equina are slow-growing and usually benign. Because the cauda equina is made up entirely of nerve filaments, the first symptom resulting from compression of the nerve roots is *pain,* which may be constant or intermittent, dull or knife-like. It may remain localized and is invariably present for many years before motor or sensory disturbances become evident. The initial onset of pain is commonly associated with a mild form of trauma or back strain. Its distribution and character may be such as to simulate lumbosacral or sacro-iliac disease. It frequently is aggravated by coughing, straining, or exertion. The pain is likely to come on at night, some hours after retiring. It is relieved by standing up and walking about, and the patient soon learns that he can be relatively free from pain if he sleeps in the sitting position.

Of the fourteen tumors occurring in the region of the cauda equina, in this series, four pathologic types deserve mention: (1) neurofibromata; (2) dislocated nucleus pulposus (chordoma); (3) epidermoids: and (4) large, soft, dural endotheliomata.

1. *Neurofibromata.* — These are slow-growing. Because these tumors arise from the sheath of a nerve root, radiating pain is the first and predominating symptom. In our patients such pain was present for as long as seven or eight years before the appearance of positive neurologic signs. Initially, it was unilateral and finally bilateral. In each instance, bilateral compression of the jugular veins reproduced the characteristic pain.

2. *Dislocated Nucleus Pulposus or Intervertebral Cartilage.* — That portion of the notocord which remains in the center of each intervertebral fibrocartilage is known as the nucleus pulposus. It is a highly elastic structure. If severe force is applied to the spine, a tear of the annulus fibrosus or a break in the intervertebral cartilage may result in a herniation of the nucleus, which may take place in one of several directions. Dorsal herniation frequently results in compression of the nerve structures. In some instances, portions of the hyaline cartilage of the disk may become separated and dislocate dorsally producing comparable effects. In either instance, repeated mild or severe trauma causes further dislocation with increased pressure on the adjacent nerve tissue.

In this series there were four cases of dislocated nucleus pulposus. The symptoms were intermittently progressive, and remissions were not uncommon. Pain, the initial symptom in each case, was of the local type and in one case was present for thirteen years before the appearance of neurologic signs, though the average duration was five and one-half years. In every case the pain simulated mild arthritis, sciatica, lumbosacral or sacroiliac strain. In three cases lipiodol localized the level of the lesion and cast the characteristic x-ray shadow of dorsal dislocation.

3. *Intradural-Epidermoid and Dermoid Tumors.* Tumors of this type are rare. In the literature they are classified as teratoma, teratoid and epi-

dermoid cysts, cholesteatoma and dermoid tumors, according to the number of germ layers present. They may occur at any point along the midline from the cephalic to the caudal extremity. Those in our series involved the cauda equina. The complex embryologic development of the rectum, anus, and caudal end of the spinal cord and its appendages, lends itself to the development of such tumors in association with bony anomalies; such association was found in two of our cases.

The delayed appearance of neurologic signs is best explained by the slow-growing character and soft content of these tumors. In one of the four cases pain was the only symptom over a period of forty-two years. The tumor measured 15 by 4 centimeters. In each instance the tumor was composed of soft, cheesy material, cholesterol crystals, and hair, the greater portion of which was encapsulated.

The reproduction of typical pain on bilateral jugular compression was present in three of the four cases. In two instances severe pain was reproduced on attempted spinal puncture. The explanation of this was found at operation. The dural sac, being completely filled by the tumor, had compressed the nerve roots against the dura so that they were directly stimulated by the needle. The production of severe pain on spinal puncture is, therefore, suggestive of a tumor which prevents dislocation of the nerve roots.

Because of the slow growth of these large, so-called giant tumors of the cauda equina, definite bony alterations can be demonstrated by x-ray examination. These alterations consist in narrowing of the pedicles, thinning of the laminae, and erosion of the posterior surfaces of the bodies of the vertebrae with resultant enlargement of the bony spinal canal.

4. *Dural Endotheliomata.*—Many of these tumors grow to enormous size and, because they are soft in consistency, produce pain for many years before the appearance of positive neurologic signs. In one instance a tumor of this type measured, before removal, 10 by 5 centimeters. In this case there were no positive neurologic findings; pain was the only complaint. The clinical and x-ray findings in these cases were comparable to those of the large dermoid tumors.

COMMENT

It is evident from a study of the cases in this series that *pain* as the initial symptom is most common. It may be localized or radiating in character. In patients in whom pain persists regardless of the treatment employed, the possibility of tumor of the spinal cord must be considered.

Early diagnosis is essential. End-results bear a direct relation to the duration and degree of motor and sensory impairment, as well as the pathologic type of the tumor.

For use in a differential diagnosis, various diagnostic aids are of value. The simplest of these is that of compression of the jugular and cervical veins. This test was applied in the last twenty-six cases in this series, and gave a positive reaction in 50 per cent. The frequency with which tumors of the conus medullaris and cauda equina simulate orthopedic disorders warrants the recommendation that this test be employed routinely in orthopedic examinations in which localized or radicular pain is present.

The test is performed readily in an office and should be carried out with the patient in both the sitting and recumbent positions. The patient is placed in a comfortable position and, when free from pain, compression of the cervical veins is made as in the familiar Queckenstedt test. As the intracranial and intraspinal pressure above the level of the block is raised, the characteristic pain may be produced if the tumor is capable of being displaced sufficiently to cause traction on or irritation of a nerve root. Although most commonly the pain is reproduced by compression of the jugular and other cervical veins, in certain instances (depending presumably on the direction in which the tumor dislocates most readily) such pain may be experienced only on sudden release of the jugular compression.

Though radicular pain is commoner in cases of tumor of the cauda equina, the value of the test is by no means limited to tumors of this region, but has proved of differential value in lesions of various pathologic types involving the cervical and thoracic portions of the spinal cord.

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DISCUSSION

CARL W. RAND, M. D. (523 West Sixth Street, Los Angeles).—I have enjoyed hearing the résumé by Doctors Naffziger and Jones of their experiences with spinal cord tumors at the University of California Medical School.

It happens that one of their cases, an hour-glass tumor of the neurofibroma type, subsequently came under my observation. The original tumor was operated upon by Dr. Howard Fleming in March, 1932. By July, 1934, there were signs of recurrence of the growth, and the patient was once more operated on September 4, 1934. The pathologic report again was a neurofibroma, and comparison with the original tumor slides showed the tissue to be identical. The tumor could only be partially removed. His remission lasted until December, 1934, when, for the third time, he was operated upon. Large portions of the tumor were again removed. The pathologic report did not indicate beginning malignancy. Another period of improvement lasted for about eight months. Upon return of paraplegia he was operated for the fourth time on August 8, 1935. At this sitting, a tumor much larger than before was found. It was removed as well as could be. The pathologist reported this material much more cellular than that removed on previous occasions, and stated "the tumor should no longer be considered neurofibroma, but neurofibrosarcoma." While patients harboring tumors of this type are usually cured by the first operative removal, this case, observed for approximately three years, shows that malignant changes may occasionally occur.

CYRIL B. COURVILLE, M. D. (312 North Boyle Avenue, Los Angeles).—This survey presents within a brief scope the essentials of the pathology and symptomatology of a group of the most hopeful surgical lesions of the central nervous system. It is indeed a tragedy of major rank in our day to permit a benign, encapsulated and enucleable dural tumor to pursue an uninterrupted course to the point of advanced and irrecoverable damage to the spinal cord. It is a tribute to the intelligence and alertness of the general practitioner that this sort of episode is now of rare occurrence.

The opportunity to study the records of fifty-nine cases of intraspinal tumor is not given to all of us, and the authors have discharged well their obligation to the pro-

fession by reporting their observations. So large a percentage of hour-glass tumors is somewhat surprising even to some of us who perhaps should be better informed. If these figures are representative, it behooves the roentgenologist to pay more attention to the relative size of intervertebral foramina in the suspected region. That we do not scrutinize critically enough the radiographs of the spine in suspected intraspinal tumors has been impressed upon me in recent years. Enlargements of the foramina, erosion of the pedicles or the lamina, and calcification or ossification within the tumor, are all too often overlooked.

Three clinical observations have proved to be helpful in my experience in the diagnosis of intraspinal tumors. The first one is now quite widely recognized, *i. e.*, the slowly and progressively ascending sensory level which may mislead the observer as to the true location of the tumor until late in the course of the condition. A second symptom, occurring typically in the ependymogliomas arising in the cervical segments of the cord, is the impairment of thermal sense in the upper extremities which stimulates the findings in syringomyelia. A third observation of interest concerns tumors of the roots of the spinal nerves with pain as the outstanding symptom. This pain is often radicular in character, occurring in spasms which become more and more frequent and severe. If sensation is tested in the area affected by the pain during the episode or immediately afterward, a typical radicular area of hypesthesia may be outlined. The finding of a xanthochromic fluid and evidences of block on the Queckenstedt test usually helps in clearing up any doubtful situations.

PITUITARY GROWTH FACTOR*

SOME CLINICAL CONSIDERATIONS

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THE growth factor was the first secretory influence to be suspected and verified in the pituitary gland. In 1885, Pierre Marie described, "a peculiar, noncongenital hypertrophy of the upper, lower and cephalic extremities," which he termed acromegaly. Two years later Minkowski suggested the rôle of the pituitary in this process. Marie, who was soon won to this point of view, felt that the disorder must be due to underfunction of the organ, if it was not a problem of intoxication rather than of aberrant secretion. His conception was natural since, at autopsy, most of the cases recorded proved to have destructive tumors in this area. While Sir Arthur Keith was first to recognize an enlargement of the sella turcica in relation to gigantism, he held much the same view as Marie regarding the processes involved. Massolongo (1892) not only argued that acromegaly and gigantism were one and the same disorder at different periods of life, but, through careful histological studies, suggested that both were the result of excessive, rather than of diminished, secretion. By the turn of the century, Hutchinson's findings of definite pituitary hyperplasia in forty-four out of forty-eight autopsied acromegalies left little doubt on this point.

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EARLY ATTEMPTS AT HYPOPHYSECTOMY

As Futcher tells us, "further knowledge of the pituitary mechanism could only be gained through experiments on the gland and the latter's fortified position in the center of the head thwarted many investigators." Early attempts at hypophysectomy, by Paulesco and others, in mature animals, had been almost invariably fatal. Cushing, whose reported work goes back to 1909, found that while extirpation of the posterior lobe alone did not produce death, total ablation ended fatally, although he felt that the fatal issue could be postponed by glandular implants. His partially hypophysectomized animals, which survived, failed to grow, and became obese and sexually dystrophic. So that even as late as 1910, most, if not all, observers felt that the gland was immediately essential to life. In that year, however, Bernard Ashner showed that immature puppies not only tolerated hypophysectomy well, but that they remained dwarfed and sexually immature. This finding was a great stimulus to experimental surgery, although the operative technique remained difficult and the mortality rate high.

CHOICE OF THE RAT AS AN EXPERIMENTAL ANIMAL

B. M. Allen and P. E. Smith, working independently, were among the first to show that removal of the buccal anlage in the tadpole resulted in cessation of growth and failure of metamorphosis into the frog. By the simple expedient of grafting bits of pituitary under the skin of the tadpole, it was then demonstrated that both growth and development were resumed. The choice of the rat as an experimental animal by Evans and Long (1921) proved a happy one. By intraperitoneal administration of fresh anterior lobe substance into numerous animals, these observers reported a consistent effect upon growth and upon the estrus cycle. It was not until Smith's discovery (1926), however, that the rat could be easily hypophysectomized, opening the way for both withdrawal and substitution experiments, that the subject received its greatest impetus. From this time on, pituitary research spread in many directions, but the process of growth continued to occupy a number of able observers. Dandy and Reichert showed that hypophysectomy can be accomplished in the dog by a new and comparatively safe operative technique. Reichert, using Evans' bovine extract intraperitoneally, was able to bring an hypophysectomized animal to a size that exceeded its normal litter mate control. Evans and his associates, using their own extract, and Putnam, Benedict and Teel, using a similar but entirely independent preparation, produced what was comparable to canine acromegaly.

CUSHING'S EFFORT TO REHABILITATE THREE PITUITARY DWARFS

During the summer of 1929, Cushing attempted the rehabilitation of three pituitary dwarfs ranging in ages from nineteen to thirty, with indifferent success. He later discovered (by testing on rats) that most of the growth promoting principle in the preparation he was using had been destroyed.